Summary of the Final report for the study

A double blind placebo controlled randomised trial to study the effects of birch pollen specific immunotherapy (BP-SIT) on the symptoms of oral allergy syndrome in adult patients

Chief Investigator

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Details of study

Full title of study:	A double blind placebo controlled randomised trial to study the effects of birch pollen specific immunotherapy (BP-SIT) on the symptoms of oral allergy syndrome in adult patients
Name of main REC:	NRES Committee South Central- Berkshire
REC reference number:	11/SC/0448
Eudract Number:	2011-004078-26
Sponsor:	Brighton & Sussex University Hospitals NHS Trust

Aims of the study

Many people with early season hay fever have problems eating fruit. This is due to a cross-reaction between proteins in pollen and proteins in tree-fruits such as apples, pears, peaches, cherries, plums etc.

It is possible to desensitise people against pollen allergy, but it is not clear whether this will alter their ability to eat apples. Previous studies had given different answers.

In our allergy service, we use a short-course vaccine to treat tree pollen allergy, with seven injections of a chemically modified pollen extract (Allergovit, produced by Allergopharma, a division of Merck).

This study aimed to find out whether treatment with Allergovit vaccine for birch pollen allergy has any effect on people's ability to tolerate apples.

Our primary end point was a change in the threshold of fresh apple than can be eaten by the subject. This was assessed using a double blind placebo controlled food challenge, and backed up by open apple challenges, using a visual analogue scale.

Achievement and Main findings

A total of 32 patients were randomised and contributed data. 17 of these were received active treatment and 15 received placebo. Mean age was 39.4 (SD 11.4); 7 were male and 25 female. 23 subjects completed the study while 9 withdrew. Seven of these withdrew consent, one was lost to follow-up and one started new medication which made them ineligible to continue.

In terms of the primary outcome, no difference was observed between the baseline and first year food challenges (p=0.276) or between the baseline and second year challenges (p=0.843). There was no discernible trend towards significance either, so we do not think we have missed a true effect due to small numbers.

On the open apple challenges, comparing year 1 to baseline, we observed a mean fall in VAS score of 20.3 points for the active group (n=10) and a drop of 15.4 points for the placebo group (n=13) (p=0.651). Similarly there was no significant difference in VAS after the open apple challenge at two years (p=0.151).

A limited number of secondary variables have been analysed. Skin test sensitivities for mid-seasonal tree pollens showed a clear reduction in the active group compared to the placebo treated group (mean reduction 5.7mm diameter relative to placebo; p=0.0024). A small reduction (not statistically significant) was seen in the early seasonal tree pollen skin tests.

No significant reductions were seen in skin sensitivity to grass pollen, apple sap or commercial apple extracts. These results are consistent with the pollens contained within the treatment vaccine and confirm that this vaccine was immunologically active, even if there was no benefit in terms of fruit tolerance.

In conclusion perhaps the most important benefit is that we can say clearly to patients with fruit-related symptoms that undergoing a course of desensitising injections (with the vaccine that we currently use) will not improve their tolerance of fresh fruit.

Future work in this area could look at better ways to quantify reactions to fruit - there is no gold standard for this and the field could benefit from a more standardised methodology for fruit challenges. Any further clinical trials of desensitisation to alleviate fruit-related symptoms would need to use clinically proven vaccines that are active against the clinical symptoms of tree pollen hay fever. New commercial vaccines are in development and it would be helpful to gather information from patients taking part in the phase III studies to see whether they notice any change in their sensitivity to apples, before embarking on any more definitive clinical trials with baseline food challenges etc.

Dissemination and publication

N.J Gray, H.E Smith, M.D. Tarzi, A.J. Frew. Double blind placebo controlled food challenges in birch oral allergy syndrome: Should they really be considered "gold standard" in clinical trials? Poster and oral presentation BSACI conference 2013

A report on the overall study outcome will be submitted to one of the forthcoming allergy meetings (most probably the BSACI annual conference) but nothing has been prepared yet

Signatures

Signature of Chief Investigator:	
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Date:	6th July 2018
Signature of sponsor representative:	
Print name:	DUNCAN FOTT.
Date:	12 July 2018.